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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,417	02/05/2004	Takuya Watanabe	2004_0003	2869

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,417	WATANABE ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *5,6,10-16 and 19* is/are withdrawn from consideration.

5)☒ Claim(s) *1* is/are allowed.

6)☒ Claim(s) *2,3,7-9,17,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 10 January 2007 has been entered in full. Claim 20 is added.

Applicant is reminded that claims 5-6, 10-16, and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 31 January 2006.

Claims 1-3, 7-9, 17-18, and 20 are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejection of claims 1-3, 7-9, and 17-18 under 35 U.S.C. § 101 (utility) as set forth at pg 4-8 of the previous Office Action (05 October 2006) is *withdrawn* in view of Applicant's persuasive arguments (10 January 2007).

2. The rejection of claim 1 under 35 U.S.C. § 112, first paragraph as set forth at pg 8 of the previous Office Action (05 October 2006) is *withdrawn* in view of Applicant's persuasive arguments regarding utility (10 January 2007).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 2-3, 7, and 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bell et al. (U.S. Patent 5,436,155). It is noted that the Examiner has interpreted claim 2 as

encompassing an infinite number of nucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 6. The basis for this rejection is set forth at pg 3-4 of the previous Office Action (05 October 2006) and at pg 12 of the Office Action of 12 April 2006.

Applicant's arguments (10 January 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

At page 7 of the Response, Applicant argues that support for "high stringent conditions" can be found in the disclosure and that it is well known in the art that hybridization under stringent conditions clearly requires a washing step. Applicant points out that a large number of US Patents have been granted with the terminology "hybridizable under stringent condition", but without the word "washing". Applicant asserts that it is well established that sequences with low percent identity will not hybridize under high stringent conditions. Applicant contends that the term "hybridizes under high stringent conditions" refers to hybridization and washing under conditions that permit only high binding of a nucleic acid molecule, such as an oligonucleotide or cDNA probe, to highly homologous sequences. Applicant concludes that the "hybridization under high stringent conditions" excludes sequences with low percent identity, such as the sequence of Bell et al.

Applicant's arguments have been fully considered but are not found to be persuasive. Claim 2 has been interpreted by the Examiner as encompassing an infinite number of nucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 6. The claim recites "[a]n isolated polynucleotide comprising a nucleotide sequence which hybridizes...". Thus, one possible interpretation of the claim is that the nucleotide sequence hybridizes to SEQ ID NO: 6, and not the polynucleotide that comprises the nucleotide sequence. Since there is no length limitation

recited in the claims for the nucleotide sequences that hybridize, the smallest possible sequence that may hybridize is two nucleotides. Bell et al. teach an isolated nucleic acid sequence that is 14.6% identical to the nucleic acid sequence of SEQ ID NO: 6 of the instant application, including nucleic acids 211-227 that are identical to nucleic acids 179-194 of SEQ ID NO: 6, thus meeting the limitations of the claims.

Additionally, each Patent Application is examined on its own merits. The invention that was deemed allowable in one patent has no bearing on this application. The claim language in the other patents may be different than that of the instant application and the "stringent condition" language recited in the claims of these other patents may have been specifically defined in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-3, 7-9, 17-18, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) an isolated polynucleotide comprising the nucleic acid sequence of SEQ ID NO: 6 and (ii) an isolated polynucleotide comprising the nucleic acid sequence which encodes the polypeptide sequence of SEQ ID NO: 5, *does not* reasonably provide enablement for an isolated polynucleotide comprising a nucleotide sequence which hybridizes under high stringent conditions to the nucleotide of SEQ ID NO: 6 wherein the conditions comprise a sodium concentration of about 19mM and a temperature at about 65°C. The specification also does not reasonably provide enablement for diagnosis or treatment of

diseases associated with expression of the polynucleotide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth at pg 9-13 of the previous Office Action (05 October 2006) and at pg 4-8 of the Office Action of 12 April 2006.

Applicant's arguments (10 January 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) At page 14 of the Response, Applicant asserts that the language "hybridization under stringent conditions" includes a washing step, and thus, the claims do not encompass an infinite number of sequences. Applicant argues that the claim language encompasses relatively few sequences.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, claim 2 has been interpreted by the Examiner as encompassing an infinite number of nucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 6. The claim recites "[a]n isolated polynucleotide comprising a nucleotide sequence which hybridizes...". Thus, one possible interpretation of the claim is that the nucleotide sequence hybridizes to SEQ ID NO: 6, and not the polynucleotide that comprises the nucleotide sequence. Since there is no length limitation recited in the claims for the nucleotide sequences that hybridize, the smallest possible sequence that may hybridize is two nucleotides. As discussed in the previous Office Action, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the hOT7T175 protein and DNA which are tolerant to change (e.g. such as by amino

acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. A large quantity of experimentation would be required by the skilled artisan to generate the infinite number of derivatives recited in the claims and screen the same for activity.

(ii) Regarding claims 8-9, at the bottom of page 14 of the Response, Applicant contends that the claims are limited to cancer. Applicant submits that Applicant has demonstrated a sufficient nexus between cancer and the present invention. Applicant argues that it would not take undue experimentation to use the present invention in the routine procedures disclosed in the art to diagnose cancer. At page 10 of the Response, Applicant asserts that the specification discloses a disease (i.e., cancer) associated with upregulated, downregulated, mutated, deleted, or translocated hOT7T175, and it does disclose the type of tissues or cells in which the polynucleotide is abnormally expressed. Applicant indicates that post-filing date references (Ohtaki et al., Masui et al., Bilban et al., Seminara et al., and WO 2004/080479) establish the relationship between the claimed invention and prevention of cancer metastasis/placenta related function and gonad related function.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification of the instant application asserts that the receptor protein is useful for prophylactic or therapeutic drug of all cancers (pg 70, lines 18-26). However, the specification of the instant application does not disclose any methods or working examples that indicate the polynucleotide of SEQ ID NO: 6 is a diagnostic or therapeutic for any diseases, including cancer. Undue experimentation would be required of the skilled artisan to determine such. For example, is the hOT7175 gene overexpressed or underexpressed in a cancer tissue sample as compared to

normal control? What expression levels must be observed in order for the skilled artisan to diagnose cancer (i.e., how high or low compared to control)? Is gene expression limited to particular tissues or types of cancers? The state of the art is also such that several factors may distort diagnostic tests, such as the distribution of different disease states among the patients, the prevalence of comorbid conditions, the range of pathologic subtypes, how disease status was classified, among others (see Tannock and Hill, The Basic Science of Oncology, 1998, McGraw-Hill: New York; pg 466-474, especially pg 470, col 1 and Table 20.1). Without more specifics about necessary sample size, cancer types, and expression level range for normal and tumor tissues, the specification has not provided the invention in a form readily usable by the skilled artisan such that significant further experimentation is unnecessary.

Additionally, as discussed in the previous Office Action, the specification does not teach any methods or working examples that indicate a hOT7T175 nucleic acid is introduced and expressed in the cell of an organism for therapeutic purposes, particularly treatment of cancer. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. The Examiner cited Phillips in the previous Office Action as evidence that gene therapy has generally been inadequate for a meaningful clinical response. Therefore, undue experimentation would be required of the skilled artisan to introduce and express a hOT7T175 nucleic acid into the cell of an organism to treat all possible cancers.

The teachings of Ohtaki et al., Masui et al., Bilban et al., Seminara et al., and WO 2004/080479 are not commensurate in scope with claims 8-9. Regarding Ohtaki et al. and Masui et al., these references simply demonstrate that the ligand, metastin, inhibits the chemotaxis and

invasion of hOT7T175-expressing *cell lines*. Bilban et al. demonstrate that a shorter peptide than metastin inhibits trophoblast migration *in vitro*. These references do not teach that administration of the DNA encoding the metastin receptor, hOT7T175, treats any cancer. These references also do not teach that hOT7T175 DNA is a diagnostic of any cancer. Although Ohtaki et al. discloses that *hOT7T175* transcripts are increased in several normal and cancerous tissue samples (see page 616, Figure 5), the specification at the time of filing does not disclose any guidance or examples to indicate that the hOT7175 gene is overexpressed or underexpressed in any cancer tissue sample or the expression levels that must be observed in order for the skilled artisan to diagnose or treat cancer. The specification only teaches that hOT7T175 is abundantly expressed in placenta and pancreas (page 6, lines 21-32).

Additionally, although Seminara et al. and WO 2004/080479 further elucidate the role of metastin and hOT7T175 in gonad regulation, this nexus was not made in the instant specification at the time of filing. These post-filing date references also generally indicate that hOT7T175 (GPR54) and metastin can be useful as anti-hormone sensitive cancer agents (abstract of WO 2004/080479) or to achieve suppression of gonadal steroids (...prostate cancer) (abstract of Seminara). However, these references, like Ohtaki et al., Masui et al., and Bilban et al., do not teach that administration of the DNA encoding the metastin receptor, hOT7T175, treats any cancer or that *hOT7T175* is a diagnostic marker.

It is noted that the courts have stated that patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may not be patentable. Tossing out the mere germ of an idea does not constitute an enabling disclosure. Reasonable detail must be provided in order to enable members of the public to understand and

carry out the invention. See *Genentech v. Novo Nordick A/S* (CAFC) 42 USPQ2d 1001 (1997).

Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, to diagnose cancer and to introduce and express a hOT7T175 nucleic acid into a cell of an organism; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; and the state of the prior art which establishes the which establishes the unpredictability of the effects of mutation on protein structure and function and the unpredictability of transferring genes into an organism's cells, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

5. Claims 2-3, 7-9, 17-18, and 20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is set forth at 13-15 of the previous Office Action (05 October 2006) and at pg 8-11 of the Office Action of 12 April 2006.

Applicant's arguments (10 January 2007), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that contrary to the Office's position, the claim language "hybridization under stringent conditions" does not encompass a large number of sequences. Applicant argues

that instead, such language encompasses relatively few sequences given that only highly homologous sequences will hybridize to the base sequence under high stringent conditions. Applicant concludes that one of skill in the art would believe that Applicant was in possession of a representative number of hybridizable sequences at the time of the invention.

Applicant's arguments have been fully considered but are not found to be persuasive. As discussed above, claim 2 has been interpreted by the Examiner as encompassing an infinite number of nucleotides that hybridize to the nucleic acid sequence of SEQ ID NO: 6. The claim recites "[a]n isolated polynucleotide comprising a nucleotide sequence which hybridizes...". Thus, one possible interpretation of the claim is that the nucleotide sequence hybridizes to SEQ ID NO: 6, and not the polynucleotide that comprises the nucleotide sequence. Since there is no length limitation recited in the claims for the nucleotide sequences that hybridize, the smallest possible sequence that may hybridize is two nucleotides.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is no identification of any particular portion or length of the structure that must be conserved. Also, the only factor present in claim 20 is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure or function that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Additionally, the description of one polynucleotide species (SEQ ID NO: 6) and one polypeptide species (SEQ ID NO: 5) is not adequate written description of an entire genus of functionally equivalent polynucleotides which incorporate all possible nucleotide sequences that hybridize to the nucleotide sequence of SEQ ID NO: 6.

Conclusion

Claim 1 is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
21 March 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER